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Studies of Morbidity in Anæsthetists with Special Reference to Obstetric History

In the course of a series of observations on the morbidity of nurses and doctors involved in operating room work in the USSR, Vaisman (1967) noted that 18 out of 32 women working in an operating theatre in the early months of pregnancy suffered spontaneous abortion. Although this was an uncontrolled observation there can be no doubt that this was a very high frequency of miscarriage and the possibility was mentioned that it might be associated with working conditions. In particular, doubts were raised about the safety of long-term inhalation of traces of anæsthetic gases and vapours. Askrog & Harvald (1970) surveyed Danish nurse anæsthetists, women anæsthetists, and the wives of male anæsthetists, although these wives had not been personally involved in operating room work, and compared their obstetric histories before and after commencement of employment in anæsthesia. The only group large enough to permit analysis was the wives of male anæsthetists who showed an approximately three-fold increase in the ratio of spontaneous abortion to total pregnancies, associated with the commencement of anæsthetic practice by their husbands. Serious criticism of this study was based on the fact that no account could be taken of the effect of age on this population.

Cohen *et al.* (1971) in a carefully controlled study of nurse anæsthetists, physician anæsthesiologists and nurse and physician pædiatricians, found that there was a three-fold increase in the frequency of spontaneous abortion apparently associated with working in an operating theatre. The study by Knill-Jones *et al.* (1972) was a further attempt to examine the effect of anæsthetic practice on obstetric history, this time with a study of much larger numbers of respondents than had been attempted previously. Questionnaires were sent to all women anæsthetists in the United Kingdom and to an otherwise comparable group of women doctors, not practising anæsthesia, randomly selected from the Medical Register. An overall reply rate of 80.5% was achieved, yielding a total of 1391 replies from married women. It was found that the frequencies of spontaneous abortions in non-anæsthetist women and in women anæsthetists who were not working during pregnancy were similar (about 14%). Women anæsthetists who were working during pregnancy had a frequency of 18.2%. The difference between this value and the values for the other two groups is statistically significant. It was found that women anæsthetists reported a two-fold increase in the frequency of involuntary infertility compared with the control group and there was also a suggestion that the frequency of congenital abnormalities was greater in the anæsthetists' group although there was no difference in the overall pattern of types of congenital abnormality. Although it was tempting to identify a triad of abortion, infertility and congenital abnormality which might all be ascribed to an abnormality of embryo development perhaps induced by anæsthetic agents, there was no direct evidence for such a suggestion and several pointers to the contrary. For example the mean maturity of abortion in both anæsthetists and control groups was similar, there was no specific system involvement to explain the increase in congenital abnormality, and of the 50% of women anæsthetists who reported a successful pregnancy following a period of

involuntary infertility, nearly all were working in an operating theatre in the early part of the pregnancy.

A study at present in progress was designed to investigate the obstetric history of the wives of male anæsthetists working in the United Kingdom and to compare them with a suitable control group, again selected randomly from the *Medical Register*. The data from this enquiry is still in the process of analysis. However it is already clear that there was no increase in the frequency of spontaneous abortion associated with the practice of anæsthesia by the father. Although the children of male anæsthetists had an increased frequency of congenital abnormalities this is accounted for by an increase in minor abnormalities, the frequency of major congenital abnormalities being equal in both groups.

The enquiry was extended further than the previous survey to include questions relating to morbidity other than that associated with childbearing. The reporting of serious illness by anæsthetists was substantially greater than that of other hospital doctors and doctors not employed in hospital practice. This increase is accounted for by an increased frequency of peptic ulceration, diseases of the cardiovascular system, heptatitis and lumbar disc disorder. These data will be the subject of further analysis and a later report. At this stage it can be said that there was no increased reporting of malignant disease of any type. This is contrary to the trend shown in the analysis of the causes of death in American anæsthesiologists (Bruce *etal.* 1968).

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Volatile Anæsthetics as Xenobiotics

Throughout the ages mammals have been exposed to many foreign chemicals or xenobiotics. Our survival has only been due to the presence of a remarkable ability of the liver to metabolize a wide variety of structurally unrelated compounds. The recent build up of environmental contamination from combustion, industrial waste, insecticides, carcinogens and other toxic chemicals has been accompanied by an ever-increasing consumption of tranquillizers, analgesics, sedatives, stimulants and narcotics. Despite all this, the expectation of life is such that we can anticipate that the major proportion of the audience will live longer than their parents. Needless to say, there are always exceptions. Our task is to try to sift the evidence for and against the specific role of exposure to anæsthetic agents as a hazard to anæsthetists.

Long-term exposures of animals to low concentrations of halothane and other volatile anæsthetics have been reported by Boba & Drews (1966), Linde & Bruce (1968) and Chenoweth *et al.* (1972). These studies are of little value as findings cannot be directly transferred to man.

Drugs are metabolized mainly in the liver. In a classical paper Conney (1967) reviewed the literature on enzyme induction and metabolism of drugs. He collected data on some 300 agents which had been shown to stimulate hepatic microsomal drug-metabolizing enzymes. These included drugs listed in Table 1.

It should be noted that these drugs belong to a wide variety of chemical groups. The principal site for their metabolism is in the smooth endoplasmic reticulum of the liver which contains the enzymes known as 'mixed function oxidases'. These require reduced nicotinamide adenine dinucleotide phosphate (NADPH) and molecular oxygen. One atom of molecular oxygen is incorporated into the organic product and the other oxygen is reduced to water. As previously mentioned, a large number of different chemical structures are dealt with by this reaction. This suggests that there is a common factor responsible for the electron transport chain.

When an enzyme-inducing drug such as phenobarbitone is administered to rats, there is proliferation of the smooth endoplasmic reticulum and an increase in liver weight. In addition, in mice given phenobarbitone, there is a decrease in sleeping time following hexobarbitone as there is proliferation of the smooth endoplasmic reticulum, increase in production of cytochrome

Table 1

Some drugs with enzyme-inducing properties

Type of Drug	*Drug*
Central nervous stimulants	Amphetamine
Hypnotics and sedatives	Barbiturates
Anæsthetics	Methoxyflurane
	Halothane
	Fluroxene
Anticonvulsants	Meprobamate
	Chlordiazepoxide
Antipsychotic	Chlorpromazine
Antihistamines	Diphenylhydramine
Hypoglycæmic agents	Tolbutamide
Anti-inflamatory agents	Phenylbutazone